CLAIMS

1. A method of ameliorating the symptoms of sepsis comprising directly exposing epithelial cells of a mammal in need thereof to an effective amount of a compound comprising soluble CD14, or a polypeptide fragment of the CD14 that stimulates expression of a defensin in epithelial cells, or a conservatively substituted variant of said CD14 or the fragment that stimulates said expression.

2. A method of enhancing expression of defensins in a mammal in need thereof, by administering a compound comprising soluble CD14 or a polypeptide portion of CD14 that enhances said expression, or a conservatively substituted variant of said CD14 or the portion that enhances said expression.

3. The method of claim 2, wherein said administering step includes directly exposing epithelial cells of the mammal to said compound.

4. A method of stimulating expression of one or more defensins by epithelial cells by administering thereto an effective amount of a compound comprising soluble CD14 or a polypeptide fragment of CD14 that stimulates said expression, or a conservatively substituted variant of said CD14 or the fragment that enhances said expression.

5. A method of stimulating expression of a defensin along the gastrointestinal tract of a mammal comprising exposing the tract to an effective amount of a compound comprising soluble CD14 or a polypeptide fragment of CD14 that stimulates said expression, or a conservatively substituted variant of said CD14 or the fragment that stimulates said expression.

6. A method of stimulating expression of a defensin along the respiratory tract of a mammal comprising exposing the tract to an effective amount of a compound comprising soluble CD14 or a polypeptide portion of CD14 that stimulates said expression, or a conservatively substituted variant of said CD14 or the portion that stimulates said expression.

7. A method of stimulating expression of a defensin on the tongue of a mammal comprising exposing the tongue to an effective amount of a compound comprising soluble CD14 or a polypeptide fragment of the CD14 that stimulates said expression, or a conservatively substituted variant of said CD14 or the fragment that stimulates said expression.

8. A method of stimulating expression of a defensin in the small intestine of a mammal comprising exposing the intestine to an effective amount of a compound comprising soluble CD14 or a polypeptide portion of CD14 that stimulates said expression, or a conservatively substituted variant of said CD14 or the portion that stimulates said expression.

9. A method of inducing expression of defensins by epithelial cells of a mammal in need thereof, the method comprising administering an effective amount of a compound comprising soluble CD14 or a polypeptide fragment of the soluble CD14 that induces said expression, or a conservatively substituted variant of said CD14 or the fragment that induces said expression.

10. The method of any preceding claim wherein the CD14 has an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7.

11. The method of claim 10, wherein the compound comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7, or a conservatively substituted variant thereof.

12. The method of claim 11, wherein the compound comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6 or SEQ ID NO:7.

13. A method of ameliorating the symptoms of sepsis comprising administering to a mammal in need thereof an effective amount of a soluble protein so as to directly expose epithelial cells of the mammal to the protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:5 and having the ability to induce expression of defensins in epithelial cells.

14. The method of claim 13 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

15. A method of prophylactically treating a lipopolysaccharide-induced host inflammatory response in a mammal, which method comprises administering a therapeutically effective amount of an effective amount of a protein to the mammal so as to directly expose epithelial cells of the mammal to the protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to enhance expression of one or more defensins in bovine epithelial cells.

16. The method of claim 15 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

17. A method of enhancing expression of defensins in a mammal in need thereof, by administering an effective amount of a soluble protein to the mammal, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability enhance expression of defensins in mammalian epithelial cells.

18. The method of claim 17 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

19. A method of stimulating expression of one or more defensins by epithelial cells by exposing the cells to an effective amount of a soluble protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to stimulate expression of one or more defensins in epithelial cells.

20. The method of claim 19 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

21. A method of stimulating expression of a defensin along the gastrointestinal tract of a mammal comprising exposing the tract to an effective amount of a soluble protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to stimulate expression of a defensin in bovine epithelial cells.

22. The method of claim 21 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

23. A method of stimulating expression of a defensin along the respiratory tract of a mammal comprising exposing the tract to an effective amount of a soluble protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to stimulate expression of a defensin in epithelial cells.

24. The method of claim 23 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

25. A method of stimulating expression of a defensin on the tongue of a mammal comprising exposing the tongue to an effective amount of a soluble protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to stimulate expression of a defensin in epithelial cells.

26. The method of claim 25 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

27. A method of stimulating expression of a defensin in the small intestine of a mammal comprising exposing the intestine to an effective amount of a soluble protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to induce expression of a defensin in epithelial cells.

28. The method of claim 27 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

29. A method of inducing expression of defensins by epithelial cells of a mammal in need thereof, the method comprising administering and effective amount of a protein, the protein having an amino acid sequence which is at least about 63% conserved in relation to the amino acid sequence identified as SEQ ID NO:4 or identified as SEQ ID NO:5 or identified as SEQ ID NO:6 and having the ability to induce expression of defensins in epthelial cells.

30. The method of claim 29 wherein the protein has an amino acid sequence which is at least about 68% or about 71% or about 73% or about 78% or about 83% or about 88% or about 93% or about 98% conserved in relation to the amino acid sequence identified as SEQ ID NO:5.

31. The method of any of claims 1 to 14 wherein the CD14 or the polypeptide portion or the variant is recombinant.

32. A method of preparing a CD14 concentrate, the method comprising:

providing a stock solution containing protein of a mammary secretion;

separating from the solution a concentrate comprising endogenous CD14; and

determining the concentration of CD14 in the concentrate.

33. The method of claim 32, wherein the mammary secretion is milk.

34. The method of claim 33, wherein the mammmary secretion is whole milk or a protein-containing portion of whole milk.

35. The method of claim 32, wherein the stock solution comprises colostrum or a protein-containing portion of colostrum.

36. The method of any of claims 32 to 35, wherein, if the secretion has been previously subjected to a treatment step, the treaunent step is sufficiently mild to permit preservation of the CD14 activity for inducing or stimulating defensin production and/or for stimulating B cells.

37. The method of any of claims 32 to 36, wherein the mammary secretion is human.

38. The method of any of claims 32 to 36, wherein the mammary secretion is bovine.

39. The method of any of claims 32 to 38, wherein the solution is a liquid solution and the separating step includes salting out of proteins from the solution.

40. The method of any of claims 32 to 39, wherein determining the concentration of CD14 includes exposing a sample obtained from the concentrate to a first antibody specific for CD14 to form an antibody-CD14 complex and subsequently exposing the complex to a second antibody specific for CD14, wherein the second antibody includes a reporter molecule.

41. The method of any of claims 32 to 39, wherein determining the concentration of CD14 includes exposing a sample obtained from the concentrate to a first antibody specific for CD14 to form an antibody-CD14 complex and subsequently exposing the complex to a second antibody specific for the first antibody, wherein the second antibody includes a reporter molecule.

42. A method of obtaining CD14, the method comprising:

providing a stock solution containing protein of a mammary secretion;

precipitating from the stock solution a protein fraction containing CD14; and

isolating the protein fraction from the supernatant.

43. The method of claim 42, wherein the precipitating step includes salting out a protein fraction containing CD14.

44. The method of claim 43, wherein the precipitating step includes increasing the salt concentration of the solution to obtain an ionic strength at least as high as would be obtained by combining a saturated aqueous solution of ammonium sulphate with a volume of a said mammary secretion, the volume of the ammonium sulphate solution being equal to 65 percent of the total volume of the combined solutions.

45. The method of any of claims 42 to 44, further comprising the step of determining the amount of CD14 obtained in the isolating step.

46. The method of any of claims 42 to 45, wherein the mammary secretion is colostrum.

47. The method of any of claims 42 to 45, wherein the mammary secretion is milk.

48. The method of any of claims 42 to 47, wherein the secretion is bovine.

49. The method of any of claims 42 to 47, wherien the secretion is human.

50. A method of obtaining CD14, the method comprising:

providing a stock solution comprising protein of a mammary secretion;

isolating from the solution a fraction containing proteins that are insoluble in the mammary secretion upon combining a saturated aqueous solution of ammonium sulphate with a volume of a said mammary secretion, the volume of the ammonium sulphate solution being equal to 65 percent of the total volume of the combined solutions.

51. The method of claim 50, further comprising the step of determining the amount of CD14 obtained in the isolating step.

52. The method of claim 50 or 51, wherein the mammary secretion is colostrum.

53. The method of claim 50 or 51, wherein the mammary secretion is milk.

54. The method of any of claims 50 to 53, wherein the secretion is bovine.

55. The method of any of claims 50 to 53, wherein the secretion is human.

56. A method for testing for the presence of CD14 in a composition containing protein of a mammary secretion, the method comprising the steps of:

exposing the composition to an antibody which is specific for CD14; and

determining whether CD14 endogenous to the secretion is present in the sample based on whether CD14-antibody complex has formed in the exposing step.

57. The method of claim 56 wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of the CD14 activity for inducing or stimulating defensin production and/or for stimulating B cells.

58. The method of claim 56 or claim 57, comprising the further step of determining the concentration of CD14 in the sample.

59. The method of any of claims 56 to 58, wherein the mammary secretion is colostrum.

60. The method of any of claims 56 to 58, wherein the mammary secretion is milk.

61. The method of any of claims 56 to 60, wherein the secretion is bovine.

62. The method of any of claims 56 to 60, wherein the secretion is human.

63. A method of preventing, ameliorating or treating the symptoms of sepsis in a mammal, comprising administering to the mammal an effective amount of CD14 obtained from a mammalian mammary secretion.

64. The method of claim 63, wherein the CD14 is obtained from bovine milk.

65. The method of claim 63 or claim 64, wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of CD14 activity for inducing or stimulating defensin production in epithelial cells.

66. The method of claim 63, wherein the CD14 is contained in a liquid.

67. The method of claim 66, wherein the liquid comprises a fraction of the milk enriched in said CD14.

68. The method of claim 63, wherein said CD14 is contained in an edible product.

69. The method of any of claims 63 to 68, wherein administering the CD14 includes exposing the gastrointestinal tract to CD14.

70. The method of any of claims 63 to 69, including adminstering the CD14 to the mammal orally.

71. A method for determining the amount of endogenous CD14 contained in a composition containing protein of a mammary secretion, the method comprising the steps of:

providing the composition;

exposing a sample of the composition to an antibody which is specific for CD14; and

determining the amount CD14 endogenous to the secretion present in the sample based on the amount of CD14-antibody complex formed in the exposing step.

72. The method of claim 71 wherein the mammary secretion is colostrum.

73. The method of claim 71 wherein the mammary secretion is milk.

74. The method of any of claims 71 to 73 wherein the secretion is bovine.

75. The method of any of claims 71 to 73, wherien the secretion is human.

76. A method for determining the suitability of a product derived from a mammary secretion for use in inducing or stimulating defensin production in mammals, the method comprising the steps of:

providing a sample of the product; and

determining the amount of CD14 present in the sample.

77. The method of claim 76, wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of the CD14 activity for inducing or stimulating said defensin production

78. The method of claim 76 or claim 77 wherein determining the amount of CD14 present in the sample includes exposing the sample to an antibody which is specific for CD14, and ascertaining whether antibody-CD14 complex is formed in the exposing step.

79. A method for determining the suitability of a product derived from a mammary secretion for use in stimulating B cells in mammals, the method comprising the steps of:

providing a sample of the product; and

determining the amount of endogenous CD14 present in the sample.

80. The method of claim 79, wherein, if the secretion has been previously subjected to a treatment step, the treatment step is sufficiently mild to permit preservation of the CD14 activity for stimulating B cells.

81. The method of claim 79 or claim 80, wherein determining the amount of CD14 present in the sample includes exposing the sample to an antibody which is specific for CD14, and ascertaining whether antibody-CD14 complex is formed in the exposing step.

82. The method of claim 79, 80 or 81, wherein the mammary secretion is colostrum.

83. The method of claim 79, 80, or 81, wherein the mammary secretion is milk.

84. The method of any of claims 79 to 83, wherein the secretion is bovine.

85. The method of any of claims 79 to 83, wherien the secretion is human.

86. The method of any of claims 1 to 12 wherein the compound is specifically recognized by an antibody which also specifically recognizes human CD14.

87. The method of claim 86 wherein the antibody is mAb 3C10 and/or a mAb that recognizes the same amino acid sequence as mAb 3C10.

88. The method of any of claims 1 to 12, or 86, the CD14 is human CD14.

89. The method of any of claims 1 to 12 or 86 to 88, including administering the compound orally.

90. The method of claim 89 wherein the compound is administered to an infant as a component of infant formula.

91. The method of any of claims 1 to 12 or 86 to 87 including administering the compound in the form of an aerosol.

92. The use of a CD14 or a compound of claim 1, in the preparation of a medicament for use in ameliorating the symptoms of sepsis.

93. The use of a CD14 or a compound of claim 2, in the preparation of a medicament for use in enhancing expression of defensins in a mammal.

94. The use of a CD14 or a compound of claim 4, in the preparation of a medicament for use in stimulating expression of one or more defensins by epithelial cells cells.

95. The use of a CD14 or a compound of claim 5, in the preparation of a medicament for use in stimulating expression of a defensin along the gastrointestinal tract of a mammal.

96. The use of a CD14 or a compound of claim 6, in the preparation of a medicament for use in stimulating expression of a defensin along the respiratory tract of a mammal.

97. The use of a CD14 or a compound of claim 7, in the preparation of a medicament for use in stimulating expression of a defensin on the tongue of a mammal.

98. The use of a CD14 or a compound of claim 8, in the preparation of a medicament for use in stimulating expression of a defensin in the small intestine of a mammal.

99. The use of a CD14 or a compound of claim 9, in the preparation of a medicament for use in inducing expression of defensins by epithelial cells of a mammal.

100. The use of a protein of claim 13 or claim 14, in the preparation of a medicament for use in ameliorating the symptoms of sepsis.

101. The use of a protein of claim 15 or 16, in the preparation of a medicament for use in prophylactically treating a lipopolysaccharide-induced host inflammatory response in a mammal.

102. The use of a protein of claim 17 or 18, in the preparation of a medicament for use in enhancing expression of defensins in a mammal.

103. The use of a protein of claim 19 or 20, in the preparation of a medicament for use in stimulating expression of one or more defensins by epithelial cells.

104 The use of a protein of claim 21 or 22, in the preparation of a medicament for use in stimulating expression of a defensin along the gastrointestinal tract of a mammal.

105. The use of a protein of claim 23 or 24, in the preparation of a medicament for use in stimulating expression of a defensin along the respiratory tract of a mammal.

106. The use of a protein of claim 25 or 26, in the preparation of a medicament for use in stimulating expression of a defensin on the tongue of a mammal.

107. The use of a protein of claim 27 or 28, in the preparation of a medicament for use in stimulating expression of a defensin in the small intestine of a mammal.

108. The use of a protein of claim 29 or 30, in the preparation of a medicament for use in inducing expression of defensins by epithelial cells of a mammal.

109 The use of a concentrate obtained according to the method of any of claims 32 to 41, in the preparation of a medicament for use in directly activating B cells.

110. The use of a concentrate obtained according to the method of any of claims 32 to 41, in the preparation of a medicament for use in directly stimulating defensin production in a mammal, particularly for the stimulation of epithelial cells for said defensin production.

111. The use of CD14 obtained according to the method of any of claims 42 to 55, in the preparation of a medicament for use in directly activiating B cells.

112. The use of CD14 obtained according to the method of any of claims 42 to 55, in the prepartion of a medicament for use in directly stimulating defensin production in a mammal, particularly for the stimulation of epithelial cells for said defensin production.

113. A method of enhancing expression of defensins in a mammal in need thereof, comprising administering to a mammal in need thereof an effective amount of a recombinant polypeptide CD14 encoded by a non-naturally occurring recombinant DNA molecule comprising a first DNA sequence selected from the group consisting of:

(a) a cDNA sequence encoding CD14 according to SEQ ID NO:2;

(b) a DNA sequence which specifically hybridizes to the noncoding strand of (a) and which codes on expression for a polypeptide specifically recognized by an antibody which also specifically recognizes human CD14; and

(c) a DNA sequence which encodes the same polypeptide as is encoded by a DNA sequence of (a) or (b) above;

wherein the polypeptide encoded by (b) or (c) enhances said expression.

114. A method of stimulating expression of one or more defensins by epithelial cells cells comprising administering to a mammal in need thereof an effective amount of a recombinant polypeptide CD14 encoded by a non-naturally occurring recombinant DNA molecule comprising a first DNA sequence selected from the group consisting of:

(a) a cDNA sequence encoding CD14 according to SEQ ID NO:2:

(b) a DNA sequence which specifically hybridizes to the noncoding strand of (a) and which codes on expression for a polypeptide specifically recognized by an antibody which also specifically recognizes human CD14; and

(c) a DNA sequence which encodes the same polypeptide as is encoded by a DNA sequence of (a) or (b) above;

wherein the polypeptide encoded by (b) or (c) stimulates said expression.

115 The method of claim 113 or 114, wherein the polypeptide is specifically recognized by an antibody which also specifically recognizes human CD14.

116. The method of claim 115 wherein the antibody is mAb 3C10 and/or a mAb that recognizes the same amino acid sequence as mAb 3C10.

117. The method of any of claims 113 to 116 including administering the polypeptide orally.

118. The method of any of claims 113 to 116 wherein the polypeptide is administered to an infant as a component of infant formula.

119. The method of any of claims 113 to 116 including administering the polypeptide in the form of an aerosol.

120. The method of any of claims 113 to 116, wherein the polypeptide is contained in concentrated milk.

121. The use of a polypeptide of claim 113, in the preparation of a medicament for use in enhancing expression of defensins in a mammal.

122. The use of a polypeptide of claim 114, in the preparation of a medicament for use in stimulating expression of one or more defensins by epithelial cells.

123. The method of any of claims 1 to 55 or 111 to 118, wherein the compound, polypeptide, protein, concentrate, or CD14, as the case may be, is added as a supplement to a dietary source.

124. The method of any of claims 1 to 4, 6, 7, 9 to 20, 23 to 26, or 29 or 30, including direct topical exposure of the epithelium of the trachea to the polypeptide or protein, as the case may be.

125. The method of any of claims 1 to 4, 13, 14, 17 to 20, or 29 or 30, including topical exposure to the outer epidermis of a mammal, particularly to wounds thereof.

126. A method of preparing an ointment for direct topical application to a wound of human skin for ameliorating the effects of infection, particularly bacterial infection, thereof, comprising incorporating into the ointment an effective amount of a concentrate obtained according to any of claims 32 to 41.

127. A method of preparing an ointment for direct topical application to a wound of human skin for ameliorating the effects of infection, particularly bacterial infection, thereof, comprising incorporating into the ointment an effective amount of CD14 obtained according to any of claims 42 to 55.

128. A dietary source such as infant formula, milk or other liquid having added thereto a fraction of a milk product, the fraction including a higher concentration of CD14 than occurs naturally in the unfractionated milk

product, wherein the milk product is one which has not been treated by a process which denatures the CD14 contained therein to the extent that CD14 loses the desired activity.

129. The dietary source of claim 128, wherein the CD14 is obtained from bovine milk.

130. Administering the dietary of source of claim 128 or 129 to a human for preventing, ameliorating or treating the symptoms of sepsis in the human.

131. Administering the dietary of source of claim 128 or 129 to a human for stimulating B cells in the human

132. Administering the dietary of source of claim 128 or 129 to a human for enhancing the expression of defensins in the human.

133. The method of claims any of claims 1 to 31 and 113 to 120, wherein the mammal is human.

134. The method of claims any of claims 1 to 31 and 113 to 120, wherein the mammal is in need of protection against a microbial pathogen selected from the group consisting of virus, bacteria, fungus and yeast.

135. The method of claims any of claims 1 to 31 and 113 to 120, where the mammal a human suffering from immune deficiency.

136. The method of any of claims 1 to 31, 65, 92 to 108 or 113 to 122, wherein the defensin(s) is selected from the group consisting of RtNP1, RtNP2, RtNP3, RtNP4, HNP1, HNP2, and HNP3 and any combination thereof, or the group consisting of HNP1, HNP2, and HNP3.

137. The method of any of claims 1 to 31, 65, 92 to 108 or 113 to 122, wherein the protein or polypeptide, as the case may be, is administered in an amount of between about 250 Tg to about 2500 Tg per kg of bodyweight of the mammal per day or in an amount of between about 300 Tg to about 1 mg per kg of bodyweight per day.

138. The method of claim 113 or 114, wherein the nucleic acid molecule having the DNA sequence of (b) hybridizes under stringent conditions to the noncoding strand of (a).

139. A method of directly activating B cells using a soluble polypeptide having the amino acid sequence selected from the group consisting of leu-leu-leu-leu-leu-leu-pro-ser; leu-leu-leu-leu-leu-leu-pro-leu; and leu-leu-leu-leu-leu-val-his, and which is specifically recognized by the monoclonal antibody 3C10 and which activates B cells, by administering to a mammal in need thereof an effective amount of said polypeptide.

140. The method of claim 139, wherein the amino acid comprises a sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6 or a conservatively substituted variant thereof which activates B cells, or a fragment thereof which activates B cells or a conservatively sustituted variant thereof which activates B cells.

141. A transgenic mammal having introduced into its genome a nucleic acid sequence encoding a polypeptide having the amino acid sequence identified as SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or fragment of said polypeptide which directly activates B cells; or a variant of said polypeptide which directly activates B cells; a conservatively substituted variant of the polypeptide; or conjugates of the fragment or variant thereof which directly activates B cells, wherein the nucleic acid sequence is under control of a CD14 promoter endogenous to the mammal and the nucleic acid sequence is in addition to nucleic acid sequences which naturally occur in the DNA of the mammal.

142. The transgenic mammal of claim 141 wherein the nucleic acid sequence encodes a polypeptide having the amino acid sequence identified as SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or fragment of said polypeptide which directly activates B cells; or a conservatively substituted variant of the polypeptide.

143. The transgenic mammal of claim 142 wherein the nucleic acid sequence encodes a polypeptide having the amino acid sequence identified as SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6, or a conservatively substituted variant of the polypeptide.

144. The transgenic mammal of claim 143 wherein the nucleic acid sequence encodes a polypeptide having the amino acid sequence identified as SEQ ID NO:4, SEQ ID NO:5, or SEQ ID NO:6.

145. The transgenic mammal of claim 144 wherein the nucleic acid sequence encodes a polypeptide having the amino acid sequence identified as SEQ ID NO:4 or SEQ ID NO:5.

146. The transgenic mammal of claim 145 wherein the nucleic acid sequence has the sequence identified as SEQ ID NO:1 or SEQ ID NO:2.

147. A transgenic mammal having introduced into its genome a nucleic acid sequence encoding a protein of claim 139 or claim 140, wherein the nucleic acid sequence is under control of a CD14 promoter endogenous to the mammal and the nucleic acid sequence is in addition to nucleic acid sequences which naturally occur in the DNA of the mammal.

148. A transgenic mammal having introduced into its genome a nucleic acid sequence encoding a protein of any of claims 1 to 31, 65, 92 to 108 or 113 or 122, wherein the nucleic acid sequence is under control of a CD14 promoter endogenous to the mammal and the nucleic acid sequence is in addition to nucleic acid sequences which naturally occur in the DNA of the mammal.

149. The transgenic mammal of any of claims 141 to 148 wherein the nucleic acid sequence is a heterologous sequence.

150. The transgenic mammal of any of claims 141 to 149 wherein the nucleic acid sequence has been introduced into the mammal or a progenitor of the mammal by recombinant technology.

151. The transgenic mammal of claim 150 wherein the nucleic acid sequence has been introduced into the mammal by recombinant technology.

152. The transgenic mammal of any of claims 141 to 151 wherein the CD14 promoter is a bovine promoter.

153. The transgenic mammal of any of claims 141 to 151 wherein the mammal is bovine.

154. A transgenic mamunal having introduced into its genome a nucleic acid sequence identified as SEQ ID NO:8, wherein the nucleic acid sequence is in addition to nucleic acid sequences which naturally occur in the DNA of the mammal.

155. The mammal of claim 154, wherein the nucleic acid sequence has been introduced into the mammal or a progenitor of the mammal by recombinant technology.

156. The mammal of claim 154, wherein the nucleic acid sequence has been introduced into the mammal by recombinant technology.

157. The mammal of any of claims 154 to 156 wherein the mammal is bovine.

158. A method of directly activating B cells using CD14 obtained according to the method of any of claims 32 to 55.